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The Pathology of Epidemic Hepatitis

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The following paper is based upon collaborative studies with Colonel Balduin Lucke of 296 autopsies from the files of the Army Institute of Pathology and of 160 biopsies from 137 cases of non-fatal hepatitis studied with Major T. H. Horan and Captain Leslie Jolliffe at the 15th Medical General Laboratory in Italy. Common to both fatal and non-fatal examples of the disease are inflammatory and degenerative changes in the liver. The former are essentially similar in all forms of the disease, but the latter differ markedly in the two groups of material.

The inflammatory process is evidenced by a conspicuous periportal and a relatively inconspicuous but constant intralobular infiltration of mononuclear cells. In the periportal connective tissues these consist of macrophages, lymphocytes, small numbers of eosinophiles and inconstant polymorphonuclear neutrophiles. They show no particular concentration about the biliary radicles. Within the lobule the infiltration is focal rather than diffuse and consists entirely of macrophages and swollen, occasionally proliferating Kupfer cells.

The degenerative changes in the liver cells

in fatal hepatitis are characterized by massive necrosis of a lytic type extending outward from the central vein to involve entire lobules or all but a few cells at the periphery of the lobule. This may develop with such rapidity that within two or three days of the onset of symptoms, even before clinical jaundice can develop, all liver cells in large areas will have completely disappeared. In less fulminant cases surviving ten or more days active regeneration develops from surviving cells at the periphery of the lobule producing macroscopic nodules of regeneration and the picture which has been termed multiple nodular hyperplasia.

The degenerative changes in non-fatal hepatitis are ordinarily entirely different in character. They consist of a coagulative necrosis of individual liver cells without obvious lobular orientation. The affected cells show first a deepening acidophilia and loss of granularity of the cytoplasm. They begin to shrink into a spherical shape, losing their attachments to adjacent cells and soon being extruded from the liver cord into the space of Desse. Meanwhile the nucleus becomes pyknotic, eccentric and finally disappears. Phagocytes accumulate about the hyaline sphere and eventually digest it.

The use of peritoneoscopic biopsy during an epidemic made it possible to study various stages of the disease in our volunteer patients. In cases studied during the prodromal period, active inflammatory and degenerative changes were already evident three to five days before the onset of jaundice and regeneration was already in progress as shown by numerous mitotic figures. A group of subicteric cases was recognized in which clinical jaundice never developed but daily serum bilirubin levels showed transient rises to levels of 1.5 to 2.0 mgm. per cent. All but one of these showed typical changes, sometimes as severe as in the frankly jaundiced cases. Finally in a non-icteric group showing neither clinical nor chemical evidence of the slightest bilirubin retention characteristics changes were found in several instances. The occurrence of non-icteric hepatitis was thereby histologically confirmed.

It was also possible to study various phases of recovery and of delayed recovery. In the average case the liver had returned to a normal or nearly normal condition three or four weeks from the onset of symptoms. Focal necrosis and intralobular inflammatory foci disappeared first, periportal infiltration more slowly. In some cases of clinically normal convalescence, however, active liver cell necrosis was still present at this period, including subicteric cases which had never shown clinical jaundice.

In cases of delayed recovery in which clinical symptoms or abnormal laboratory findings persisted weeks and months after the subsidence of jaundice histologic evidence of persistent activity was also usually obvious. One case still hospitalized for persistent symptoms two and one half years after his original attack showed active inflammation and fresh focal necroses in a recent biopsy and no significant change from a specimen secured one year ago. One final group of ten cases deserves mention. Clinically diagnosed chronic hepatitis without jaundice on the basis of persistent symptoms and palpable livers but without abnormal laboratory findings and with no history of an acute attack, the biopsies uniformly failed to show changes characteristic of hepatitis.

(SECTION ON MICROBIOLOGY CONTINUED ON NEXT PAGE)